

Applicant gratefully acknowledges the withdrawal of the rejection of all of the claims (claims 1, 2 and 5-25) as obvious over Musser.

Claims 1, 2 and 5-14 and 16-25 stand rejected as obvious over Berger (U.S. Patent No. 5,713,376) in view of Musser. With respect to this rejection, the Office Action indicates that it would have been prima facie obvious for one of ordinary skill in the art to reduce the amount of nicotine in the tobacco plants to a non-addictive level as taught by Berger, by applying glucose oxidase as taught by Musser. The concentration of glucose oxidase or the necessary number of treatments to achieve non-addictive levels is stated to be well within the skill of the art. The person skilled in the art, it is further stated, would be motivated to achieve non-addictive levels in order to produce a cigarette product that is non-addictive as taught by Berger. The rejection is hereby traversed and reconsideration is respectfully requested.

Musser is stated to teach that saliva produced by the salivary glands of a caterpillar *H. zea* reduces the amount of nicotine released by the tobacco plant (page 599, first paragraph). Nicotine inhibits the growth of *H. zea* and therefore the reduction in nicotine enables the caterpillar to ingest the plant minimizing adverse effects. The reduction in nicotine is to a level of about 26% compared with a control (page 599, middle column, lines 9-10). This degree of reduction of nicotine is sufficient to prevent harm to the caterpillar.

The Office Action has previously acknowledged that the reference fails to teach or suggest the desired amount of treatment required to obtain a non-addictive level of nicotine. The withdrawal of the rejection based on Musser alone is indicative that it was not obvious to proceed with what is taught in Musser to arrive at the claimed invention. The Office Action now relies on Berger to teach lowering nicotine levels to non-addictive levels and concludes that utilizing the process of Musser for this purpose would be routine and non-patentable. The rejection is hereby traversed and reconsideration is respectfully requested.

Applicant agrees that Berger teaches non-addictive levels of tobacco. However, fundamental to the discussion of obviousness is how Berger reaches such non-addictive levels. The Berger process involves converting the nicotine of a tobacco product into a harmless and actually beneficial substance, such as nicotinic acid (column 2, line 66 to column 3, line 2). In this regard, Berger treats the nicotine existing in the tobacco plant with chemical reactants to convert the nicotine into neutral or beneficial compounds. Thus, Berger takes tobacco plants which have a full compliment of nicotine and treats those plants with substances that can convert the nicotine to harmless byproducts. By way of example, nicotine in the tobacco product is converted to nicotinic acid by means of an oxidizing agent, such as nitric acid (column 3, lines 54-56). Other oxidizing agents are listed at column 3, lines 57-61.

Musser does not use a chemical reactant such as an oxidizing agent to reduce the full complement of nicotine in a tobacco plant to a lower amount by converting at least some of the nicotine to a harmless byproduct. Quite to the contrary, Musser reduces the amount of harmful nicotine released by the tobacco plant by use of an enzyme (glucose oxidase) which "counteracts the production of nicotine induced by the caterpillar feeding on the plant". Thus, Musser does not convert nicotine to a harmless byproduct (nicotine acid), but instead notes that nicotine production can be inhibited by the use of the glucose oxidase enzyme emanating from the caterpillar.

The combination of Musser and Berger does not lead one of ordinary skill in the art to the present invention. In its broadest teaching, Berger indicates that low levels of nicotine can be obtained from plants which have their full complement of nicotine (i.e. there is no attack on nicotine production) by treating the tobacco leaves with oxidizing substances that convert at least some of the already produced nicotine to harmless byproducts through the use of a chemical reactant. Musser teaches that certain caterpillars excrete an enzyme (non-reactant) which inhibits nicotine production in a tobacco plant to a point where the amount of nicotine produced in the plant does not adversely affect the caterpillar.

Berger therefore only provides the skilled artisan with a desire to achieve low level nicotine tobacco products. Absent using oxidants to react with existing nicotine, Berger does not provide any guidance to one of ordinary skill in the art to

modify what is fairly taught in Musser. Instead, the person of ordinary skill in the art would, as previously explained, understand that the use of enzymes to inhibit production of staple products in biological systems is system specific and non-stoichiometric and therefore lacks predictability. Enzyme based systems are distinctly different than the Berger system where chemical stoichiometric reactions convert nicotine to a harmless byproduct. Applicant has previously established that one of ordinary skill in the art would not routinely expect that further treatments of the enzyme glucose oxidase on live tobacco plants would achieve non-addictive levels of nicotine. To achieve non-addictive levels of nicotine the skilled artisan would look to a chemical reaction type system of Berger which converts existing nicotine to harmless byproducts (such reactions are quantitative or stoichiometric). There is no rationale in the prior art to use enzyme based systems for this purpose.

It is therefore submitted that the combination of Musser and Berger does not lead one of ordinary skill in the art to the present invention.

Claim 15 has been rejected as obvious over the combination of Berger and Musser further in view of the Hibi publication. In connection with this rejection, the Office Action acknowledges that neither Berger nor Musser teach reducing the level of nicotine in a genetically modified tobacco plant that exhibits reduced nicotine levels as compared to a non-genetically modified tobacco plant. It is further stated that genetic engineering of tobacco plants for the purpose of reducing nicotine levels

is known in the art and that Hibi teaches genetically modified tobacco plants with reduced levels of nicotine.

The Office Action concludes that it would have been prima facie obvious for one skilled in the art to apply glucose oxidase to genetically modified tobacco plants which already have reduced levels of nicotine in order to obtain a tobacco product with non-addictive levels of nicotine. The rejection is hereby traversed and reconsideration is respectfully requested.

Neither Musser nor Hibi teach a tobacco product with levels of nicotine that are so small that they can be considered non-addictive. As we have previously shown, the combination of Berger and Musser would not lead one of ordinary skill in the art to the claimed invention.

Hibi teaches a series of experiments to suggest that Nic 1 and Nic 2 are regulatory genes for nicotine biosynthesis. However, given this teaching, one of ordinary skill in the art would still not be led to the invention of claim 15 which is the only claim rejected based on Hibi. This is because Hibi does not teach a method of reducing nicotine in tobacco plants. The reference has identified regulatory genes for nicotine biosynthesis but has not offered a method by which non-addictive levels in tobacco plants can be achieved. Given that Hibi does not teach any particular reduced levels of nicotine in tobacco plants, the citation of Musser for the proposition that adding glucose oxidase to genetically engineered tobacco plants would result in


ARK:jsg082307/1631004.RES

non-addictive levels of nicotine is not based on the reference teachings and is pure speculation given the reference content. Knowing what genes may be involved in nicotine biosynthesis is not a teaching of how to obtain tobacco products of the present invention. We have previously shown that Musser does not teach or suggest a method by which such low levels of nicotine can be obtained by tobacco plants. This is Applicant's discovery and such discovery is neither anticipated nor rendered obvious by the combination of references cited in the present application.

In view of the foregoing, Applicant submits that the present application is in condition for allowance and early passage to issue is therefore deemed proper and is respectfully requested.

It is believed that no fee is due in connection with this matter. However, if any fee is due, it should be charged to Deposit Account No. 23-0510.

Respectfully submitted,


Allen R. Kipnes, Esquire
Registration No. 28,433
Attorney for Applicant

Address All Correspondence to:

Allen R. Kipnes, Esquire
WATOV & KIPNES, P.C.
P.O. Box 247
Princeton Junction, NJ 08550
(609) 243-0330